WHAT IS CLAIMED IS:

1. A polyclonal antisera composition of a nonhuman animal that specifically recognizes an immunogen, wherein said antisera composition is comprised predominantly of substantially human immunoglobulin protein molecules comprised of at least a portion of a human heavy chain polypeptide, wherein said substantially human immunoglobulin protein molecules specifically bind to said immunogen.

2. The polyclonal antisera according to Claim 1, wherein said transgenic nonhuman animal is immunized with said antigenic entity, weighs at least 1 kg and comprises at least a portion of functional human heavy chain immunoglobulin genes integrated by homologous recombination into its genome.

3. The polyclonal antisera composition according to Claim 1, wherein said transgenic nonhuman animal generates antibody diversity predominately by gene conversion.

4. The polyclonal antisera composition according to Claim 1, wherein said transgenic nonhuman animal is from the order *Lagomorpha*.

5. The polyclonal antisera composition according to Claim 1, wherein said portion of functional human heavy chain immunoglobulin genes comprises at least one constant region element.

6. The polyclonal antisera composition according to Claim 5, wherein said portion of functional human heavy chain immunoglobulin genes further comprises at least one variable region element.

7. The polyclonal antisera composition according to Claim 6, wherein said variable region element is the variable region element proximal to the D region.

8. The polyclonal antisera composition according to Claim 1, wherein said immunogen

~~comprises a disease causing organism or antigenic portion thereof.~~

9. The polyclonal antisera composition according to Claim 1, wherein said immunogen is an antigen endogenous to humans.

10. The polyclonal antisera composition according to Claim 1, wherein said immunogen is an antigen exogenous to humans.

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11. A transgenic nonhuman animal weighing at least 1 kg and comprising at least a portion of functional human heavy chain immunoglobulin genes integrated by homologous recombination into its genome, wherein said portion of functional human heavy chain immunoglobulin genes rearranges in frame with heavy chain immunoglobulin sequences endogenous to said nonhuman animal to encode functional, substantially human antibody molecules that comprise at least in part human heavy chain immunoglobulin polypeptide sequences, and wherein said animal predominantly produces said functional, substantially human antibody molecules when immunized.

12. A transgenic nonhuman animal weighing at least 1 kg and comprising at least a portion of functional human light chain immunoglobulin genes integrated by homologous recombination into its genome, wherein said human light chain immunoglobulin genes rearrange in frame with sequences endogenous to said nonhuman animal to encode functional, substantially human antibody molecules that comprise at least in part human light chain immunoglobulin polypeptide sequences.

13. The transgenic nonhuman animal according to Claim 11, ~~wherein said transgenic nonhuman animal~~ generates antibody ~~diversity~~ predominately by gene conversion.

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14. The transgenic nonhuman animal according to Claim 11, wherein said ~~transgenic~~ nonhuman animal is from the order *Lagomorpha*.

15. The transgenic nonhuman animal according to Claim 11, wherein said portion of functional human heavy chain immunoglobulin genes comprises at least one constant

region element.

16. The transgenic nonhuman animal according to Claim 15, wherein said portion of functional human heavy chain immunoglobulin genes further comprises at least one variable region element.

17. The transgenic nonhuman animal according to Claim 16, wherein said variable region element is the variable region element proximal to the D region.

18. The transgenic nonhuman animal according to Claim 12, wherein said human immunoglobulin light chain gene encodes the κ chain.

19. An antisera composition produced by the transgenic nonhuman animal according to Claim 11.

20. A method for neutralizing an antigenic entity in a human body component, said method comprising:
contacting said body component with an antisera composition according to Claim 1, whereby said substantially human immunoglobulin protein molecules in said antisera composition specifically bind and neutralize said antigenic entity.

21. The method according to Claim 20, wherein said antigenic entity is from an organism that causes an infectious disease.

22. The method according to Claim 20, wherein said antigenic entity is a cell surface molecule.

23. The method according to Claim 22, wherein said cell surface molecule is from a lymphocyte or an adipocyte.

24. The method according to Claim 20, wherein said antigenic entity is a human cytokine or a human chemokine.

25. The method according to Claim 20, ~~wherein said antigenic entity is a cell surface molecule~~ on a malignant cancer cell.

Sub a5

26. A method of producing a transgenic nonhuman animal weighing at least 1 kg and comprising human immunoglobulin genes integrated by homologous recombination into its genome, wherein said animal predominantly produces functional, substantially human antibody molecules comprised at least in part of human immunoglobulin polypeptide sequences when immunized, said method comprising:

producing a first mutated animal comprising heavy chain immunoglobulin loci where constant and/or variable region elements are replaced with at least a functional portion of the human heavy chain immunoglobulin locus by genetic alteration of a cell nucleus of said animal, introducing said cell nucleus into an enucleated nuclear transfer unit cell to provide a first embryonic stem cell, introducing said first nuclear transfer unit cell into a female recipient host to produce a first mutated neonate;

producing a second mutated animal comprising light chain immunoglobulin loci where constant and/or variable region elements are replaced with at least a functional portion of the human light chain immunoglobulin locus by genetic alteration of a cell nucleus of said animal, introducing said cell nucleus into an enucleated nuclear transfer unit cell to provide a second embryonic cell stem cell, introducing said second nuclear transfer unit cell into a female recipient host to produce a second mutated neonate; and

breeding mature first and second mutated neonates and selecting animals capable of producing substantially human antisera and being at least substantially incapable of producing endogenous antisera.

27. A method of producing a transgenic nonhuman animal weighing at least 1 kg and comprising human immunoglobulin genes integrated by homologous recombination into its genome, wherein said animal predominantly produces functional, substantially human antibody molecules comprised at least in part of human immunoglobulin polypeptide sequences when immunized, said method comprising:

producing a mutated animal comprising heavy and light chain immunoglobulin loci where constant and/or variable region elements are replaced with at least a

functional portion or the human heavy and/or light chain immunoglobulin locus by genetic alteration of a cell nucleus of said animal, introducing said cell nucleus into an enucleated nuclear transfer unit cell to provide a embryonic cell stem cell, introducing said nuclear transfer unit cell into a female recipient host to produce mutated neonate; and

breeding mature mutated neonates and selecting animals capable of producing substantially human antisera and at least substantially incapable of producing endogenous antisera.

28. The method according to Claim 26, wherein said nuclear transfer unit cell is an oocyte.

29. The method according to Claim 26, wherein said animal is from the order of *Lagomorpha*.

sub a6 30. A method according to Claim 26, wherein said heavy chain locus comprises ~~at least one~~ constant region element.

31. A method according to Claim 26, wherein said heavy chain locus comprises at least one variable region element.

32. A method according to Claim 26, wherein said heavy chain locus comprises the variable region element proximal to the D region.

add a7